



Nebraska Department of Health and Human Services



HEALTH ALERT NETWORK Advisory



TO: Nebraska Healthcare Providers & Laboratories

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RE: Tick Borne Diseases in Nebraska

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The movement of humans to the great outdoors during the spring and summer seasons leads to concerns among patients and health care providers regarding tick borne disease. This article addresses the three tick-borne diseases known to be present in Nebraska, and discusses other possible tick-borne diseases, whose presence in Nebraska is unproven and which require cooperation between patients, doctors and public health officials to define their epidemiology.

The three well-characterized tick-borne illnesses endemic to Nebraska are Rocky Mountain spotted fever, ehrlichiosis, and tularemia. Unproven tick borne diseases of interest which require further study to determine their presence and extent in Nebraska are Lyme disease, caused by *Borrelia burgdorferi* and transmitted by *Ixodes scapularis* ticks, anaplasmosis (formerly called human granulocytic ehrlichiosis) caused by *Anaplasma phagocytophilum*, and a Lyme-like illness potentially associated with *Borrelia lonestari* or other *Borrelia* spp.

The two tick species believed to be associated with these diseases in Nebraska are *Dermacentor variabilis* and *Amblyomma americanum*. *Ixodes scapularis* (formerly *Ixodes dammini*) is the only known vector of *Borrelia burgdorferi* and *Ehrlichia phagocytophila*, the causative agents of Lyme disease and anaplasmosis, respectively. This tick has never been detected in Nebraska: its absence makes indigenous acquisition of Lyme disease and anaplasmosis highly suspect.

Rocky Mountain spotted fever (RMSF)

RMSF has long been endemic in Nebraska, with fewer than ten cases reported every year. Because RMSF occurs infrequently in Nebraska, health care providers might overlook this diagnosis. RMSF should be a diagnostic consideration in any person with a fever and a history of exposure to environments where ticks might be present. The skin rash which gives this illness its name is not always present when the patient first presents to a physician. This disease is easily unrecognized and misdiagnosed, with numerous reports of serious and sometimes fatal consequences. Laboratory diagnosis is made by detecting a rise in antibody titer to *Rickettsia rickettsii* between acute and convalescent sera. The organism can also be detected using fluorescent antibody methods on tissue biopsy since the organism infects the endothelium. The disease responds to tetracycline-class of antibiotics and chloramphenicol. Immediate empiric therapy is recommended and should not be delayed while awaiting diagnostic results.

Ehrlichiosis

Ehrlichiosis is caused by *Ehrlichia chaffeensis*, an intracellular bacterium that grows within cytoplasmic phagosomes of white blood cells, and can cause leukopenia. Presumptive diagnosis can be made by identifying the classic inclusion or morulae in the cytoplasm of monocytes or macrophages. While a review of the peripheral blood smear can suggest the diagnosis, confirmation requires a four-fold rise in IgG antibody titer between acute and convalescent sera or by molecular detection of *Ehrlichia* DNA in clinical specimens.

The symptoms of this disease include a maculo-papular rash as well as fever and chills. The illness may progress with hypotension, coagulopathy, hemorrhage of internal organs and renal failure. Prior to 1986, ehrlichiosis was a veterinary diagnosis affecting horses or dogs and caused by organisms related to the human pathogen, *E. chaffeensis*.

Tularemia

Tularemia is a disease of animals and humans caused by the gram negative bacterium *Francisella tularensis*. Rabbits, hares, and rodents are especially susceptible and often die in large numbers during outbreaks. Humans can become infected through several routes, including tick or deer fly bites, skin contact with infected animals, bites from infected cats, ingestion of contaminated water, or inhalation of contaminated dusts or aerosols.

Illness from *F. tularensis* ranges from mild to life-threatening. Disease is accompanied by fever, which can be as high as 104°F. Disease following a tick bite or deerfly bite is usually ulceroglandular and is the most common form of tularemia. A skin ulcer appears at the site where the organism entered the body, and is typically accompanied by swelling of regional lymph glands, usually in the armpit or groin. Tularemia can present without an ulcer, the so-called "glandular form." Diagnosis can be made by isolation of *F. tularensis* in a clinical specimen or by a four-fold rise or greater change in serum antibody titer to *F. tularensis* antigen. Although tularemia can be life-threatening, most infections are successfully treated with antibiotics.

Lyme Disease

Lyme disease, caused by a spirochete called *Borrelia burgdorferi*, is now the most prevalent tick-borne disease in the United States. This organism is transmitted by the tick *Ixodes scapularis* which has never been identified in Nebraska. This fact makes any diagnosis of Nebraska-acquired Lyme disease caused by *B. burgdorferi* highly suspect. Lyme disease is highly regional in the United States (http://www.cdc.gov/ncidod/dvbid/lyme/ld_incidence.htm). As a result of a long-established rule for assigning reportable diseases to the patient's state of residence, some confusion regarding the distribution of Lyme disease exists: persons who have had out-of-state exposure to ticks in highly endemic areas are reported by states where classic Lyme disease is not thought to occur. The situation in Nebraska is a classic example: in 2009 we reported four such cases to the national reportable disease system at the CDC. All had out-of-state exposure.

Further confusion exists regarding the endemic acquisition of Lyme disease in Nebraska because of technical issues with the diagnostic tests. Two laboratory diagnostic approaches are used to confirm the diagnosis of Lyme disease: serologic tests looking for antibody to *B. burgdorferi*, and tissue culture or other molecular detection methods. There has never been a tissue culture or other molecular/antigenic confirmation of *B. burgdorferi* in a person suspected of indigenous acquisition of Lyme disease in Nebraska. However, every year Nebraska's state and local public health agencies receive reports of Nebraskans whose serologic test for Lyme disease was reported as positive. While some of these persons reported a tick-prone exposure in regions of the country where classic Lyme disease is clearly established and likely represent true cases of Lyme disease, many of these persons have never left Nebraska. The positive Lyme disease

serology in this latter group of patients is likely explained by a lack of specificity of the laboratory tests. These are likely false-positive tests. They may reflect underlying medical conditions such as rheumatoid arthritis, or prior exposure to other spirochetal organisms similar to *B. burgdorferi* that lead to a cross reaction with the Lyme serologic test (e.g.s, *Leptospira* species, treponemal species, or *Borrelia* species other than *B. burgdorferi*).

Current recommendations for serologic testing for Lyme disease are to perform an initial ELISA test, which if positive should be followed by a Western blot. The Western blot should include an IgG and IgM assay. A positive Western blot is required as part of the diagnosis. The assays have greatly improved sensitivity and specificity in untreated patients tested two to three weeks following exposure. IgM positivity is transient, and if present greater than four weeks following exposure is likely to be a false-positive. The extent to which current serologic tests may cross-react with *Borrelia* species other than *B. burgdorferi* (such as "*Borrelia lonestari*") is not established.

Southern Tick-Associated Rash Illness (STARI)

One notable example of cross-reactivity with the Lyme disease serologies is the recently recognized existence of a poorly characterized *Borrelia*-like organism felt to be transmitted by *Amblyomma americanum*, often referred to as the Texas lone-star tick. This tick, which is common in southern and central Nebraska (as far West as North Platte), has been reported to harbor a *Borrelia* species different from *B. burgdorferi*. Researchers are currently attempting to characterize this organism and its life cycle, and to develop tissue culture and serologic tests. Infection with this organism, known as *Borrelia lonestari*, may cause a clinical syndrome similar to Lyme disease, including erythema migrans skin lesions. The full spectrum of its clinical manifestations is currently poorly defined. It appears that persons believed to be infected with this organism have milder illness and fewer long-term sequelae compared to persons infected with *B. burgdorferi*. The suspected infection appears to respond to antibiotics used to treat Lyme disease.

While this disease might be endemic to Nebraska, its occurrence is speculative and unproven. We have never identified this spirochete in tick or human samples collected in Nebraska. Whether the lesion and illness described in patients following an *Amblyomma americanum* tick bite is infectious or allergic/toxin mediated is speculative.

Work in Progress: We Need Your Help

Nebraska's state and local health departments need the assistance of patients and doctors to accurately define the spectrum of tick-borne disease in Nebraska. People who want ticks identified should contact our office to make arrangements (Dr. Annette Bredthauer 402-471-1374 Annette.Bredthauer@nebraska.gov). Physicians who suspect non-endemic tick-borne disease (e.g., Lyme disease, anaplasmosis, or STARI-related disease) should contact a public health official (Tom Safranek, M.D., State Epidemiologist or Dr. Bryan Buss 402-471-2937) for assistance in a diagnostic work-up. Lesions consistent with erythema migrans found in Lyme disease should undergo punch biopsy of the leading edge of the skin lesion with tissue sent for culture and diagnostic testing at CDC, together with serologic testing. PCR can be done on CSF, synovial fluid, or skin punch biopsy. Details for specimen collection and transport can be obtained by contacting the Nebraska Public Health Laboratory (Toll-Free: 1-866-290-1406; Call Pager: 402-888-2086).

TICK	DISTRIBUTION	ASSOCIATED ILLNESS	INFECTIOUS AGENT
<i>Dermacentor variabilis</i> (American dog tick or wood tick)	Statewide	Rocky Mountain spotted fever Human monocytic ehrlichiosis Tularemia	<i>Rickettsia rickettsii</i> <i>Ehrlichia chaffeensis</i> <i>Francisella tularensis</i>
<i>Amblyomma americanum</i> (Texas lone star tick)	Southern and central Nebraska	Human monocytic ehrlichiosis Variant Lyme disease	<i>Ehrlichia chaffeensis</i> “ <i>Borrelia lonestari</i> ”
<i>Ixodes scapularis</i> (deer tick)	Never identified in Nebraska	Lyme disease Human granulocytic ehrlichiosis	<i>Borrelia burgdorferi</i> <i>Ehrlichia phagocytophila</i>